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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,056	03/22/2004	Laura L. Kiessling	1-00A	1530

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BOULDER, CO 80301

EXAMINER

SHIBUYA, MARK LANCE

ART UNIT	PAPER NUMBER
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1639

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09/06/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/806,056	Applicant(s) KIESSLING ET AL.	
	Examiner Mark L. Shibuya, Ph.D.	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 6/18/2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,48,53,65,67,78,79,88-91,93,95,99-103,106,108,109 and 149-177 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 1,48,53,65-69,78,79,82-84,88-93,95,99-106,108-111,116,117,119-121,123-126 and 128-177.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 66,68,69,82-84,92,104,105,110,111,116,117,119-121,123-126 and 128-148.

DETAILED ACTION

1. Application 10806056, (20040248801 A1): Claims 1, 48, 53, 65-69, 78, 79, 82-84, 88-93, 95, 99-106, 108-111, 116, 117, 119-121, 123-126 and 128-177 are pending.

Claims 66, 68, 69, 82-84, 92, 104, 105, 110, 111, 116, 117, 119-121, 123-126, and 128-148 are withdrawn from consideration.

Claims 1, 48, 53, 65, 67, 78, 79, 88-91, 93, 95, 99-103, 106, 108, 109, and 149-177 are examined.

Election/Restrictions

2. Applicant's election with traverse of the Invention of Group II, claims 67, 78-88 and 93, (and claims 2-88, 90-94, 96-99 and 102-109), drawn to methods of inducing a biological response, comprising an ATRP polymer, in the reply filed on 3/26/2007, is acknowledged. The traversal is on the ground(s) that it is unclear. Applicant request clarification of the restriction requirement with respect to claims 89 and 101 and their dependent claims. This is not found persuasive because claims 89 and 101 are linking claims, (see Requirement for Restriction/Election, mailed 9/26/2006, at pp. 6-7).

Applicant elected the claims of Group II to the extent that they are directed to methods employing an atom-transfer radical polymerization. Applicant observed that the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowed linking claims will

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be rejoined. Therefore the examiner respectfully submits that the restriction requirement is not unclear.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement regarding Groups III, IV, V and VI, the election in regards to Groups III, IV, V and VI has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election with traverse of the species of (1) immune adherence; (2) a biological system comprising an erythrocyte and a species such as an antigen or pathogen which is to be subjected to immune adherence which could be in a system in vitro or in vivo; (3) a receptor on an erythrocyte and more specifically CR1; (4) a species that recognizes and binds to a receptor on an erythrocyte and more specifically an anti-CR1 Fab'; (5) a species of binding recognition element that binds to a pathogen or antigen, including an antibody or fragment thereof and more specifically an anti-pathogen Fab'; (6) a type of binding of SRE to a scaffold that is covalent binding; (7) a species of molecular scaffold that is an ATRP polymer which is a methyl acrylate polymer and wherein the polymer contains one or more maleimide species, as in scheme 13; (8) an ultimate species of multivalent ligand that is the species of Example 7 and Figure 21 and as illustrated in schemes 13 and 14, which is a maleimide-containing methyl acrylate polymer which carries an anti-staphylococcus aureus Fab' and an anti-CR1 Fab'; in the reply filed on 3/26/2007, is acknowledged. The traversal is on the ground(s) that the various species of each generic method claim of Group II are linked by the generic claims 1, 89, 95 and 101 among others and that one or more of

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these generic claims are believed to be allowable and as such the election should be withdrawn. This is not found persuasive because the examiner respectfully submits that the said generic claims are not allowable.

The requirements are still deemed proper and are therefore made FINAL.

3. Claims 66, 68, 69, 92, 110, 111, 116, 117, 119-121, 123-126, and 128-148 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Claims 82, 105, and 106 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/26/2007.

Applicant, in the Reply entered, at p. 21, states that claims 1, 48, 53, 53, 65, 67, 78, 79, 88-91, 93, 101, 103, 108, 109, 119, 120, 123-126, 128-132, 134-177 read on the elected species.

Priority

4. This application, 10/806,056, filed 3/22/2004, claims benefit of 60/456,778, filed 3/21/2003, and states that it is a continuation-in-part of 09/815,296, filed 3/21/2001, which claims benefit of 60/191,014, filed 3/21/2000.

5. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/815,296, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application No. 09/815,296, (20030125262 A1), does not disclose atom-transfer radical polymerization (ATRP), immune adherence, and CR1. Therefore, to the extent that the claimed invention encompasses methods comprising atom-transfer radical polymerization (ATRP), immune adherence, and CR1, the effective filing date is the filing date of provisional application 60/456,778, filed 3/21/2003.

Specification

6. The abstract of the disclosure is objected to because it has more than 150 words. Correction is required. See MPEP § 608.01(b).

7. The disclosure is objected to because of the following informalities: Compound 21 in Scheme 2 appears to fall within the amino acid sequence rules, and so must be

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provided a sequence identifier number ("SEQ ID No."). Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1, 48, 53, 65, 67, 78, 79, 88, 93, 95, 99, 100, 108, 109, and 149-160, 166 and 167 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and its dependent claims, recite the language "and bonded to a molecular scaffold", which renders the claims indefinite, because it is unclear as to whether it is the multivalent ligand or the at least one receptor that is bonded to the molecular scaffold.

Claims 67, 93, 100, 166, and 167 recite the terms ATRP, which is an abbreviation; the claims must provide the words for which this term stands.

Claims 78, 79, 88 and 108 recites the terms SRE and RE, which are abbreviations; the claim must provide the words for which these terms stand.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1, 48, 53, 65, 89-91, 95, 99, 101-103, 106, 108, and 109 are rejected under 35 U.S.C. § 102(b) as being anticipated by Whitesides et al., WO 98/46270 A2.

The claims are drawn to methods for inducing a biological response in a biological system comprising one or more receptors which comprises the step of introducing into the biological system a multivalent ligand which comprises a plurality of signal recognition elements recognized by at least one of the receptors, wherein the plurality is bonded to a molecular scaffold.

Whitesides, throughout the publication and at p. 3, lines 11-24, p. 7, lines 24-31, p. 14, lines 1-9, p. 15, lines 20-31, teaches multivalent ligands on a polymeric backbone of the form $Y-(A)_n$, where Y is a framework, A is a functional group, and n is an integer greater than 10, 50 or more, or about 100 or more and wherein the functional group that is a signal recognition is covalently bonded to the framework that is a molecular

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scaffold, such as a liposome; teaches at p. 32, lines 7-13, polyvalent presenters that include Sialyl Le^x that bind leukocyte receptor sites including integrins and selectins and are elements involved in signal recognition, inducing intracellular and intercellular responses; teaches at p. 60, line 26-p.61, line 20 modulation of cell-cell interactions by polyvalent presenters, (which include multivalent ligands), whereby numerous cell-cell interactions can be promoted or inhibited, such as neutrophil attachment to endothelial cells during inflammation; teaches at Table 2, p. 62, line 4-p. 63, line 7, cell-cell interactions that include neutrophil, endothelial cells, T-cells, and the release of platelet granules; teaches at p. 87, lines 3-18, teaches cytokine production by replacing a stimulator cell in a cell-cell interaction that normally leads to cytokine secretion, e.g., the L-selectin ligands to simulate monocytes and macrophages to produce tumor necrosis factor; teaches at p. 96, line 1-p. 99 line 16, *in vitro* assays; at p. 97, line 31- p. 99, line 16, teaches cross-linking multivalent receptors on the cell by agglutinins to prevent the biological response of viral binding to the cell surface.

Whitesides et al., at pp. 18-20, Table 1, disclose polymethacrylate polymers and subunits derived from maleic anhydride or malic acid. Whitesides et al., at p. 38, disclose "preactivation" methods comprising succinimide compounds. Whitesides et al., at pp. 63-75 and Tables 3 and 4, disclose modulation of infection and teach receptors for pathogens. Whitesides et al., at pp. 131-138, Table 10, disclose agglutination assays comprising polyvalent polymers inhibiting the adhesion of ricins to erythrocytes.

Whitesides et al., at p. 24, teach functional groups for tracking by providing a label that can be detected, e.g., by fluorescent or radioactive tag. Whitesides et al., at

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p. 36, lines 9-22, teach solid supports, such as beads. Whitesides et al., at pp. 70-72, teach bacterial pathogens. Whitesides et al., at p. 30, line 23, teaches a Group A ligand that is abciximab, reading on an antibody and a Fab fragment.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

13. Claims 1, 48, 53, 65, 67, 78, 79, 88-91, 93, 95, 99-103, 106, 108, and 109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitesides et al., WO 98/46270 A2, and Brocchini et al., WO 01/18080 A1.

Whitesides et al. is relied upon as above.

Whitesides et al. does not teach a polymer scaffold that is an atom-transfer radical polymerization (ATRP) scaffold.

Brocchini et al., WO 01/18080 A1, throughout the publication and abstract, teach functionalized polymers, including polymeric multivalent ligands made by atom-transfer radical polymerization (ATRP). Brocchini et al., at pp. 17-24, teach ATRP polymers having the formulae of claim 78.

It would have *prima facie* obvious for one of ordinary skill in the art at the time of the invention to combine methods for inducing biological response by multivalent ligands with a multivalent ligand polymer wherein the polymer scaffold that is an atom-transfer radical polymerization (ATRP) scaffold.

One of ordinary skill in the art would have been motivated to use with a multivalent ligand polymer wherein the polymer scaffold that is an atom-transfer radical polymerization (ATRP) scaffold because Brocchini et al., at p. 1, lines 3-8, teach that such scaffolds are a class of polymer precursors with narrow molecular weight distribution and the production therefrom of physiologically soluble polymer

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therapeutics, functionalized polymers, pharmaceutical compositions and materials, all with similar molecular weight characteristics and a narrow molecular weight distribution.

14. Claims 149-177 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitesides et al., WO 98/46270 A2, and Brocchini et al., WO 01/18080 A1, as applied to claims 1, 48, 53, 65, 67, 78, 79, 88-91, 93, 95, 99-103, 106, 108, and 109 above, and further in view of Taylor et al., WO 03/007971 A1.

Whitesides et al., WO 98/46270 A2, and Brocchini et al., WO 01/18080 A1, are relied upon as above.

Neither of Whitesides et al. or Brocchini et al., WO 01/18080 A1, teach methods comprising ligand polymers comprising immune adherence, CR1 and Fab' fragments.

Taylor et al., WO 03/007971 A1, throughout the publication and abstract, and at pp. 1-2, teach heteropolymer complexes comprising antibodies specific for CR1 receptor in methods based upon the phenomena of immune adherence. Taylor et al., at p. 21, teach Fab' antibody fragments specific for CR1. Taylor et al., at p. 26, teach crosslinking antibodies using maleimide functional groups.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the invention to combine methods of inducing biological response by multivalent ligands that bind to receptors, with methods comprising ligand polymers comprising immune adherence, CR1 and Fab' fragments.

One of ordinary skill in the art would have been motivated to use methods comprising ligand polymers comprising immune adherence, CR1 and Fab' fragments because Taylor et al., at pp. 5-9, teach the use of antibodies against CR1 expressed on erythrocytes in primates can dramatically affect the efficiency of the complex to clear pathogens or immunogens or antigens that bind to CR1, and because Taylor teach the use of such methods for detecting the presence of an antigen or pathogen in a mammal.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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16. Claims 1, 48, 53, 65, 89-91, 95, 99, 101-103, 108, and 109 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17, 21-23, 28-30, 41-43, 59-61, 63-65, 68-74, 89-92, 140-148, 150, and 156-163 of copending Application No. 09/815,296. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of the instant application drawn to methods for inducing a biological response in a biological system comprising a multivalent ligand which comprises a plurality of signal recognition elements bonded to a molecular scaffold is obvious over the claims of 09/815,296, drawn to methods for inducing the release of an intracellular signal that induces cellular chemotaxis, reading on a biological response, comprising a multivalent ligand comprising signal recognition elements bonded to a molecular scaffold that is a ring-opening metathesis polymerization scaffold. The examiner respectfully submits that the instant provisionally rejected claims are drawn to a genus that encompass the species of methods claimed in copending Application No. 09/815,296.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

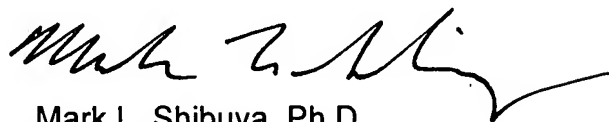
17. Claims 1, 48, 53, 65, 67, 78, 79, 88-91, 93, 95, 99-103, 106, 108, 109, and 149-177 are rejected.

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18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya, Ph.D. whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mark L. Shibuya, Ph.D.
Primary Examiner
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